## DETAILED ACTION

This supplemental action replaces the previous Final action sent 4/28/2010, and restart the time for response.

### Status of the Claims

Claims 1-15 are presented for examination on the merits.

**Withdrawal of Rejection:**

In view of amended claims and applicant's argument, the rejection under 35 USC, 112-2nd paragraph, and the rejection under 35 USC, 102(a) over Sanders, 102(b) over Asai, and Kulisek, and the rejection under 35 USC, 103(a) over Kulisek and Graham are hereby withdrawn.

The amendments to Drawings and Specification are accepted.

**New rejections due to amendment to the claims**:

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: claim 1 lacks a correlating step to accomplish the preamble of the claim.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 5, 6, 8, 9, 11, 12-15 are rejected under 35 U.S.C. 102(b) as being anticipated by Wolf (1996).

Wolf teaches a method for detecting of proteolytic microorganisms from mixed populations using a Remazol Brilliant Blue R (CAS# 2580-78-1 same as Reactive blue No. 19, see attached SnagIt FDA approval Doc) labeled casein (casein-RBB, gelatin-RBB, collagen-RBB, dye-labeled substrates) for proteinase activity (page 339, left column, 1st paragraph, page 340, left column, 1st full paragraph, and Fig. 5 on page 341).

Therefore, Wolf teaches a method (**Claims 1)** for detecting proteolytic microorganisms (page 341, Fig. 5) by **a)** exposing an casein-RBB (in agar plate, page 340, left column, 1st full paragraph) to a sample of mixed microbial (page 340, right column, line 1-4) ; and **b)** detecting cleaving of the peptide that results in clearing of blue agar plate (page 341, Fig. 5, a visible color change); wherein the substrate is specifically cleaved by proteinase produced by *Verticillium lecanii*, etc. (page 341, Fig. 5 legend, read as microorganism); wherein the dye is a remazol dye (Remazol Brilliant Blue) approved by FDA; the dye Remazol Brilliant Blue is covalently bonded to the peptides (page 339, left column, 2nd paragraph, line 5, **Claim 2**); wherein the modification includes hydrolysis of a peptide bond and results in a portion of the peptide detaching from the substrate (proteolytic activity of microorganism, page 341, left column, lines 2-3, lines 11-12, **Claim 3**); wherein the dye is Remazol Brilliant Blue: a reactive fiber dye (page 338, left column, 2nd paragraph, lines 2-3, **Claim 5**); wherein the visible color change is a loss of blue color in the agar plate (page 341, Fig. 5, **Claim 6);** the peptide substrate is coupled into agar plate as solid support (**Claim 8,** agarose read as resin- **Claim 11**, page 339, left column, 1st paragraph); wherein the cleavage of the substrate results in a hue of the agar plate becoming more visible

(page 341, fig. 5, **Claim 9);** and the sample tested is a well of microplate/agar plate (because the mixture of microbial population is added to the agar plate wells, page 340, right column, line 1-2, **Claim 12**); wherein the cleavage of the substrate inherently results in the migration of the cleaved portion of the peptide that resulting in the clearing of the blue agar plate (page 341, Fig. 5, **Claim 13**), therefore the agar plate (read as resin) is considered the collector **(Claim 14**); the method identifies protease from bacteria *Verticillium lecanii*, etc., (page 341, Fig. 5 **Claim 15).**

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 4, 7, 8, 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Wolf and Sanders (WO03/063693).

Wolf teaches what is above as applied to claims 1, 8.

Wolf does not teach the substrate listed in claim 4, the substrate is further includes a second colorimetric component that is dissimilar to the first colorimetric component, the peptide is covalently attached to the solid support.

Sanders teaches a method for detecting the modification of a peptide substrate by exposing an unmodified dye (for example, **two different dyes**: edans (5-((2-aminoethyl) amino)naphthalene-1-sulfonic acid and dabcyl 994-(4-(dimethylamino)phenyl)azo)benzoic acid see page 43, , **Claim 7)** labeled peptides (peptide substrates PAPA1/PALA1/PAGA1, page 42, example 13, and peptide substrate PAPA1 has the same sequence as SEQ ID NO:2 of the instant application, **Claim 4)** substrate on a solid support: wound dressing ( page 4 lines 1-3, such as a wound dressing-page 26, 4$^{th}$ full paragraph, **Claim 10)** to a wound sample.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Wolf by substituting substrate-casein/collagen/gelatin with other peptide sequence such as SEQ ID NO:2 of the instant application and label it with two dyes for the detection of the specific microorganism producing the protease that cleave their specific substrate because Wolf teaches the detection of the proteolytic microorganisms with labeled substrate. One would have been motivated to make the modification because Wolf et al. specifically described a loss of color for detection of proteolytic microorganisms, and would reasonably have expected success in view of Sanders' teachings because they both use chromogenic assay in bacteria detection.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

**Maintenance of Rejection:**

***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 8, 11, 15 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 16, 18, 20, 35, 37, 39, 53, 57 of copending Application No. 10502882. Although the conflicting claims are not identical, they are not patentably distinct from each other because the same method steps are claimed where the instant application detects color change specifically (narrower). Therefore, the claims of the instant application are rendered obvious in view of those (broader claims) of the copending application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The double patenting rejection maintained until a terminal disclaimer is filed and approved.

Applicant's arguments are moot in view of the new art rejections necessitated by the amendments.

## ***Conclusion***

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

No claim is allowed.

Art of record: Wang (2003 Feb) teaches labeling of peptide with vinyl sulfones as probe for cysteine protease assay (page 738, Scheme 1).

Any inquiry concerning rejections or objections in this communication or earlier communications from the examiner should be directed to Bin Shen, whose telephone number is (571) 272-9040. The examiner can normally be reached on Monday through Friday, from about 9:00 AM to about 5:30 PM. A phone message left at this number will be responded to as soon as possible (i.e., shortly after the examiner returns to her office).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached at (571) 272-0925.

*B Shen*
Art Unit 1657

/JON P WEBER/

Supervisory Patent Examiner, Art Unit 1657